THE JOHNS HOPKINS UNIVERSITY

Hemit

SCHOOL OF HYGIENE AND PUBLIC HEALTH 615 North Wolfe Street Baltimore, Maryland 21205, U.S.A.

DEPARTMENT OF BIOCHEMISTRY

February 28, 1978

(301) 955-3671

Dr. Joshua Lederberg Joseph D. Grant Professor of Genetics School of Medicine Stanford University Stanford, California 94305

Dear Josh:

I am responding to your request of February 7, '78 for recollections about your report to the Cold Spring Harbor Symposium in the summer of 1946. You are perhaps too young to recognize that memories play tricks as one gets old but I have a fairly vivid memory of you on that day.

You were dressed in khaki pants and shirt opened at the neck - and during the morning session you stood in the rear of the room with a clipboard in your hand and after each speaker had finished you asked several questions As he answered them you checked them off your list. This repeated questioning by a young person may have irritated the big speakers which included Jaques Monod and other invited guests. My recollection is that you spoke in the afternoon and Max Delbruck sat on the front row reading a newspaper (probably The New York Times). Lwoff and Monod were on the front row also and one or the other interrupted you several times commenting on the low frequency of recombinants. You reported of the order of 10^{-5} - 10^{-6} (as I remember). They indicated that such frequencies were so insignificant as to suggest nothing. As I recall you claimed that your controls showed a much lower frequency so the frequency of the recombinants was highly significant. I don't recall their bringing up the transformation concept but that doesn't mean it wasn't. I thought you were very uncomfortable at times but you stuck by your data.

I was irritated that Ed Tatum wasn't there to give you some support and turn the front row jury from a negative attitude to a positive one in which they would try to understand your phenomena rather than to destroy it as probably wrong.

I fear that some of this may be imaginary on my part except that all three of the high priests were known to be strongly opinionated and to be outspoken on occasion.

I don't recall Delbruck saying anything but his reading of the paper on the front row was either extremely bad manners or his way of putting a young person in his place.

This adds nothing to science but it does show how some scientists behave. Unfortunately many young people mimic their high priests when they are halfway up the ladder and this perpetuates an unfortunate attitude.

As an aside, I would like to say I never saw this attitude in Al Hershey. He has always impressed me as a fair, considerate person.

Turning to Wyatt's article it is a little difficult for me to judge who did not appreciate the significance of Avery's discovery for I was so close to it. I think what happened was that after World War II when many physicists or phys-chemists came off the Manhattan project and were looking for something very different to tackle, they were encouraged by the Cal Tech-Delbruck School to get into phage work for there they could do quantitative studies and examine both genetic and viral processes. Thus Stent, Benzer, Szillard and others got into the field. Stent either failed to read the literature which included Avery's study or he forgot, for he went overboard when the Hershey Chase experiment was reported. The Hershey-Chase study had all the problems that Avery had but which Stent ignored. The injectable material of the phage had several percent protein as well as nucleic acid. In the meantime Hotchkiss had reduced the protein content of Transforming Principle to so low a value, without loss of transformation activity, that the protein was ruled out. This seems to have been missed by many readers. The very good experiments of McCarty using deoxyribonuclease clinched it for me. Stent appears not to have appreciated the work of Avery's laboratory and was abruptly reminded of it by Carl Lamanna.

I am not surprised that many did not immediately accept Avery's original report as proof positive. Mirsky was quite right in pointing to the protein content of Avery's preps. Northrop once told me he could give me a solution which I would be unable to find chemically anything in it but water, yet he could dilute it a million fold and produce infection. This merely emphasized that the possibility - not the probability existed that the protein might still be a key component.

However, the Hershey Chase was the frosting on the cake that attracted Stent and others. It was a good experiment (I actually started it myself until I heard that Hershey was finished with it) but results were not compelling.

I have thought of writing this for publication but there has been so much written on it I doubt if it would add much that is new.

Perhaps this is not different from your own recollections.

Regards!

Roger M. Herriott

Professor of Biochemistry

RMH: gh